REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

The specification has been amended to make reference to government support with which this invention was made.

Claim 25 has been amended to make explicit that which was implicit (i.e., that the "patient" is a human patient and that "the sample from said patient " is a biological sample). Further, claim 25 has been amended to include the limitations of now cancelled claim 26. On page 14 of the Action, the Examiner contends that the Amendment filed October 2, 2006 "does not point to support in the instant specification for the generic teachings of a transmembrane helix or an intracellular loop." Respectfully, the Examiner appears to have overlooked the comments at page 7, lines 7 and 8 where Applicant stated "[m]ore specifically, transmembrane helices and intracellular loops of α_{1a}AR (recited in claim 25 and claims depending therefrom) are shown in Figure 2." With references throughout the application to SNPs within particular transmembrane helices and intracellular loops (see, for example, pages 18, 19, and 21, and Tables 7 and 8), there can be no doubt but that support exists. Claims 27 and 29 have been revised to depend properly from claim 25. In addition to claim 26, claims 8-24, 31 and 32 have also been cancelled without prejudice. That the claims have been revised/cancelled should not be taken as an indication that Applicant agrees with any position taken by the Examiner. Rather the revisions have been made merely to advance prosecution and Applicant reserves the right to pursue any deleted subject matter in a continuation application. New claims 36 and 37 have been added and find support, for example, at page 25, lines 26-28.

The Examiner indicates on page 3 of the Action that claims 27, 28 and 32 are withdrawn from consideration. This withdrawal is based on the Examiner's assertion that each DNA polymorphism is patentably distinct. That assertion is made here for the first time. It is noted that should a generic claim be found to be allowable, Applicant will be entitled to the species encompassed by claims 27 and 28 (claim 32 has been cancelled).

Claims 25, 26, 29, 31 and 33-35 stand rejected under 35 USC 112, first paragraph, as allegedly lacking written description. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

On page 6 of the Action, and in response to Applicant's prior arguments, the Examiner states "the claim remains drawn to any polymorphism which affects the amino acid sequence of the gene". Respectfully, such is not the case.

The claims encompass point mutations that result in an amino acid substitution in a specified region of α_{1a}AR. As now presented, claim 25 is limited to point mutations in TM4, TM5, TM7 or the third IL (Figure 2 provides the seven-transmembrane spanning model of human α_{1a}AR showing the primary amino acid sequence.) As detailed in Lei et al (2005) (of record), two SNPs (R166K and V311I) (in TM4 and TM7, respectively) cause a decrease in binding affinity for agonists norepinephrine, epinephrine, and phenylephrine, and also shift the dose-response curve for norepinephrine stimulation of inositol phosphate (IP) production to the right (reduced potency) without altering maximal IP activity. In addition, SNP V311I and I200S (in TM5) display altered antagonist binding. A receptor with SNP G247R (located in the third intracellular loop) displays increased maximal receptor IP activity and stimulates cell growth. The increased receptor signaling for α_{1a}AR G247R is not mediated by altered ligand binding or a deficiency in agonist-mediated desensitization, but appears to be related to enhanced receptor-G

protein coupling. Thus, four naturally-occurring human α_{1a}AR SNPs clearly induce altered receptor pharmacology and/or biological activity.

The scope of the claims as presented is entirely consistent with the written description provided, including the specific examples of mutations. Accordingly, reconsideration is requested.

Claims 25, 26, 29-31 and 33-35 stand rejected under 35 USC 112, first paragraph, as allegedly being non-enabled. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

In rejecting the claims as non-enabled, the Examiner again contends that the art teaches a lack of association between mutations of α_{1a}AR and diseases. As pointed out previously, none of the references cited by the Examiner relates to point mutations that result in amino acid changes in the regions of the receptor recited in the claims as now presented. The references upon which the Examiner relies relate generally to non-coding sequences or sequences encoding the C-terminus (e.g, Bolonna et al and Sofowera et al). As regards the C-terminus, attention is directed to Price et al, J. Biol. Chem. 277:9570 (2002) cited in the application at page 14. This reference teaches that acute agonist-mediated desensitization of human α_{1a}-AR is primarily independent of the carboxy terminus. The Examiner's reliance on Meyer et al is not understood as Meyer et al is concerned with the CADPKL gene and no basis is seen for the Examiner's apparent assertion that Meyer et al's findings are applicable to α_{1a}AR. Clarification is requested. Similarly, the Examiner is requested to clarify how the generalities of the Hirschhorn et al and Ioannidis et al are relevant to the specific subject matter of the instant claims.

The Examiner also states (pages 10-11 of the Action) that the specification provides no express definition of what makes a sequence an α_{1a}AR gene sequence. The Examiner goes on to

state that the claims are not limited to human biological samples. Claim 25 as presented is now so limited. As regards what makes a sequence an α_{1a}AR gene sequence, the Examiner is reminded that the application includes innumerable citations to articles that include teachings relevant to the α_{1a}AR gene. This is plainly a designation well known and widely used in the art. Accordingly, no basis is seen for the Examiner's suggestion that its meaning is in any way unclear.

On page 13 of the Action, the Examiner indicates that Applicant's arguments regarding the cited references are not convincing. The only justification given for this comment is that "the claims, namely claim 32 encompasses the C-terminus, although claim 31 does not include the C-terminus."

This comment is not understood for two reasons. First, the rejection includes claim 25 which refers to TM helicies and an intracellular loop. These domains are not in the C-terminus. Further, claim 32 does not encompass the C-terminus. As pointed out on page 7 of the Amendment filed October 2, 2006, Table 6 identifies residue 347 and residues C-terminal thereto as being "C-terminus". Claim 32 requries that the substitution be N-terminal to residue 347, therefore, not within the C-terminus.

In addition to the above, the Examiner's attention is directed to the fact that meaningful conclusions as to associations between mutations and diseases must be based on samples of such size as to enable appropriate statistical analysis, which is not the case in all of the references cited by the Examiner.

The Examiner comments that the mutation at 247 is not present in black or caucasian individuals, thus, detecting disease using the polymorphism in such individuals would be unpredictable. No basis for this assertion is seen. If the polymorphism is not present in a patient

sample, be that patient Hispanic or non-Hispanic, no disease detection results from the practice of the claimed method.

The Examiner also comments that the specification does not specifically analyze any of the polymorphisms with any of the diseases. In response, Applicant directs the Examiner's attention to pages 21-25, particularly, page 25, only full paragraph.

In view of the foregoing, the Examiner is urged to reconsider and withdraw the rejection.

Claims 25, 26, 39 [???], 31 and 33-35 stand rejected under 35 USC 112, first paragraph, as allegedly lacking written description. Withdrawal of the rejection is in order in view of the cancellation of claim 31 and further in view of the comments that follow.

No basis for the rejection of claims 25 and claims depending therefrom is seen. As pointed out above, Applicant directs the Examiner's attention to, for example, Figure 2 where support for the reference to transmembrane helix or intracellular loops is found (see too the description of this Figure in the paragraph bridging pages 3 and 4). Further, and also as pointed out above, the disclosure includes innumerable references to the transmembrane helices and intracellular loop locations of the described SNPs.

In view of the above, the Examiner is requested to provide support for the rejection or withdraw same.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

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Respectfully submitted,

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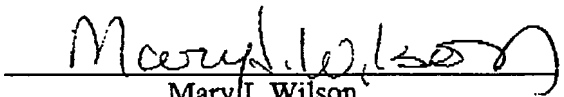
By: 
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